



SEQUENCE LISTING

<110> TUSZYNSKI, MARK
BLESCH, ARMIN

<120> MUTANT PRO-NEUROTROPHIN WITH IMPROVED ACTIVITY

<130> 041673/2045

<140> 09/788,188

<141> 2001-02-16

<160> 16

<170> PatentIn Ver. 2.1

<210> 1

<211> 241

<212> PRT

<213> Homo sapiens

<400> 1

Met Ser Met Leu Phe Tyr Thr Leu Ile Thr Ala Phe Leu Ile Gly Ile
1 5 10 15

Gln Ala Glu Pro His Ser Glu Ser Asn Val Pro Ala Gly His Thr Ile
20 25 30

Pro Gln Val His Trp Thr Lys Leu Gln His Ser Leu Asp Thr Ala Leu
35 40 45

Arg Arg Ala Arg Ser Ala Pro Ala Ala Ala Ile Ala Ala Arg Val Ala
50 55 60

Gly Gln Thr Arg Asn Ile Thr Val Asp Pro Arg Leu Phe Lys Lys Arg
65 70 75 80

Arg Leu Arg Ser Pro Arg Val Leu Phe Ser Thr Gln Pro Pro Arg Glu
85 90 95

Ala Ala Asp Thr Gln Asp Leu Asp Phe Glu Val Gly Gly Ala Ala Pro
100 105 110

Phe Asn Arg Thr His Arg Ser Lys Arg Ser Ser Ser His Pro Ile Phe
115 120 125

His Arg Gly Glu Phe Ser Val Cys Asp Ser Val Ser Val Trp Val Gly
130 135 140

Asp Lys Thr Thr Ala Thr Asp Ile Lys Gly Lys Glu Val Met Val Leu
145 150 155 160

Gly Glu Val Asn Ile Asn Asn Ser Val Phe Lys Gln Tyr Phe Phe Glu
165 170 175

Thr Lys Cys Arg Asp Pro Asn Pro Val Asp Ser Gly Cys Arg Gly Ile
180 185 190

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Asp Ser Lys His Trp Asn Ser Tyr Cys Thr Thr Thr His Thr Phe Val
 195 200 205

Lys Ala Leu Thr Met Asp Gly Lys Gln Ala Ala Trp Arg Phe Ile Arg
 210 215 220

Ile Asp Thr Ala Cys Val Cys Val Leu Ser Arg Lys Ala Val Arg Arg
 225 230 235 240

Ala

<210> 2
 <211> 241
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Mutant NGF
 pro-neurotrophin

<400> 2
 Met Ser Met Leu Phe Tyr Thr Leu Ile Thr Ala Phe Leu Ile Gly Ile
 1 5 10 15

Gln Ala Glu Pro His Ser Glu Ser Asn Val Pro Ala Gly His Thr Ile
 20 25 30

Pro Gln Val His Trp Thr Lys Leu Gln His Ser Leu Asp Thr Ala Leu
 35 40 45

Arg Arg Ala Arg Ser Ala Pro Ala Ala Ala Ile Ala Ala Arg Val Ala
 50 55 60

Gly Gln Thr Arg Asn Ile Thr Val Asp Pro Arg Leu Phe Lys Lys Arg
 65 70 75 80

Arg Leu Arg Ser Pro Arg Val Leu Phe Ser Thr Gln Pro Pro Arg Glu
 85 90 95

Ala Ala Asp Thr Gln Asp Leu Asp Phe Glu Val Gly Gly Ala Ala Pro
 100 105 110

Phe Ser Arg Thr His Arg Ser Lys Arg Ser Ser Ser His Pro Ile Phe
 115 120 125

His Arg Gly Glu Phe Ser Val Cys Asp Ser Val Ser Val Trp Val Gly
 130 135 140

Asp Lys Thr Thr Ala Thr Asp Ile Lys Gly Lys Glu Val Met Val Leu
 145 150 155 160

Gly Glu Val Asn Ile Asn Asn Ser Val Phe Lys Gln Tyr Phe Phe Glu
 165 170 175

Thr Lys Cys Arg Asp Pro Asn Pro Val Asp Ser Gly Cys Arg Gly Ile
 180 185 190

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Asp Ser Lys His Trp Asn Ser Tyr Cys Thr Thr Thr His Thr Phe Val
 195 200 205
 Lys Ala Leu Thr Met Asp Gly Lys Gln Ala Ala Trp Arg Phe Ile Arg
 210 215 220
 Ile Asp Thr Ala Cys Val Cys Val Leu Ser Arg Lys Ala Val Arg Arg
 225 230 235 240
 Ala

<210> 3
 <211> 247
 <212> PRT
 <213> Homo sapiens

<400> 3
 Met Thr Ile Leu Phe Leu Thr Met Val Ile Ser Tyr Phe Gly Cys Met
 1 5 10 15
 Lys Ala Ala Pro Met Lys Glu Ala Asn Ile Arg Gly Gln Gly Gly Leu
 20 25 30
 Ala Tyr Pro Gly Val Arg Thr His Gly Thr Leu Glu Ser Val Asn Gly
 35 40 45
 Pro Lys Ala Gly Ser Arg Gly Leu Thr Ser Leu Ala Asp Thr Phe Glu
 50 55 60
 His Val Ile Glu Glu Leu Leu Asp Glu Asp Gln Lys Val Arg Pro Asn
 65 70 75 80
 Glu Glu Asn Asn Lys Asp Ala Asp Leu Tyr Thr Ser Arg Val Met Leu
 85 90 95
 Ser Ser Gln Val Pro Leu Glu Pro Pro Leu Leu Phe Leu Leu Glu Glu
 100 105 110
 Tyr Lys Asn Tyr Leu Asp Ala Ala Asn Met Ser Met Arg Val Arg Arg
 115 120 125
 His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser Ile
 130 135 140
 Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met Ser
 145 150 155 160
 Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly Gln
 165 170 175
 Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr Thr
 180 185 190
 Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln Cys
 195 200 205

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Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys Lys
210 215 220

Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys Thr
225 230 235 240

Leu Thr Ile Lys Arg Gly Arg
245

<210> 4

<211> 247

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Mutant BDNF
pro-neurotrophin

<400> 4

Met Thr Ile Leu Phe Leu Thr Met Val Ile Ser Tyr Phe Gly Cys Met
1 5 10 15

Lys Ala Ala Pro Met Lys Glu Ala Asn Ile Arg Gly Gln Gly Gly Leu
20 25 30

Ala Tyr Pro Gly Val Arg Thr His Gly Thr Leu Glu Ser Val Asn Gly
35 40 45

Pro Lys Ala Gly Ser Arg Gly Leu Thr Ser Leu Ala Asp Thr Phe Glu
50 55 60

His Val Ile Glu Glu Leu Leu Asp Glu Asp Gln Lys Val Arg Pro Asn
65 70 75 80

Glu Glu Asn Asn Lys Asp Ala Asp Leu Tyr Thr Ser Arg Val Met Leu
85 90 95

Ser Ser Gln Val Pro Leu Glu Pro Pro Leu Leu Phe Leu Leu Glu Glu
100 105 110

Tyr Lys Asn Tyr Leu Asp Ala Ala Ser Met Ser Met Arg Val Arg Arg
115 120 125

His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser Ile
130 135 140

Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met Ser
145 150 155 160

Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly Gln
165 170 175

Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr Thr
180 185 190

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Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln Cys
 195 200 205
 Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys Lys
 210 215 220
 Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys Thr
 225 230 235 240
 Leu Thr Ile Lys Arg Gly Arg
 245

<210> 5
 <211> 257
 <212> PRT
 <213> Homo sapiens

<400> 5
 Met Ser Ile Leu Phe Tyr Val Ile Phe Leu Ala Tyr Leu Arg Gly Ile
 1 5 10 15
 Gln Gly Asn Asn Met Asp Gln Arg Ser Leu Pro Glu Asp Ser Leu Asn
 20 25 30
 Ser Leu Ile Ile Lys Leu Ile Gln Ala Asp Ile Leu Lys Asn Lys Leu
 35 40 45
 Ser Lys Gln Met Val Asp Val Lys Glu Asn Tyr Gln Ser Thr Leu Pro
 50 55 60
 Lys Ala Glu Ala Pro Arg Glu Pro Glu Arg Gly Gly Pro Ala Lys Ser
 65 70 75 80
 Ala Phe Gln Pro Val Ile Ala Met Asp Thr Glu Leu Leu Arg Gln Gln
 85 90 95
 Arg Arg Tyr Asn Ser Pro Arg Val Leu Leu Ser Asp Ser Thr Pro Leu
 100 105 110
 Glu Pro Pro Pro Leu Tyr Leu Met Glu Asp Tyr Val Gly Ser Pro Val
 115 120 125
 Val Ala Asn Arg Thr Ser Arg Arg Lys Arg Tyr Ala Glu His Lys Ser
 130 135 140
 His Arg Gly Glu Tyr Ser Val Cys Asp Ser Glu Ser Leu Trp Val Thr
 145 150 155 160
 Asp Lys Ser Ser Ala Ile Asp Ile Arg Gly His Gln Val Thr Val Leu
 165 170 175
 Gly Glu Ile Lys Thr Gly Asn Ser Pro Val Lys Gln Tyr Phe Tyr Glu
 180 185 190
 Thr Arg Cys Lys Glu Ala Arg Pro Val Lys Asn Gly Cys Arg Gly Ile
 195 200 205

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Asp Asp Lys His Trp Asn Ser Gln Cys Lys Thr Ser Gln Thr Tyr Val
 210 215 220
 Arg Ala Leu Thr Ser Glu Asn Asn Lys Leu Val Gly Trp Arg Trp Ile
 225 230 235 240
 Arg Ile Asp Thr Ser Cys Val Cys Ala Leu Ser Arg Lys Ile Gly Arg
 245 250 255

Thr

<210> 6
 <211> 257
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Mutant NGF
 pro-neurotrophin

<400> 6
 Met Ser Ile Leu Phe Tyr Val Ile Phe Leu Ala Tyr Leu Arg Gly Ile
 1 5 10 15
 Gln Gly Asn Asn Met Asp Gln Arg Ser Leu Pro Glu Asp Ser Leu Asn
 20 25 30
 Ser Leu Ile Ile Lys Leu Ile Gln Ala Asp Ile Leu Lys Asn Lys Leu
 35 40 45
 Ser Lys Gln Met Val Asp Val Lys Glu Asn Tyr Gln Ser Thr Leu Pro
 50 55 60
 Lys Ala Glu Ala Pro Arg Glu Pro Glu Arg Gly Gly Pro Ala Lys Ser
 65 70 75 80
 Ala Phe Gln Pro Val Ile Ala Met Asp Thr Glu Leu Leu Arg Gln Gln
 85 90 95
 Arg Arg Tyr Asn Ser Pro Arg Val Leu Leu Ser Asp Ser Thr Pro Leu
 100 105 110
 Glu Pro Pro Pro Leu Tyr Leu Met Glu Asp Tyr Val Gly Ser Pro Val
 115 120 125
 Val Ala Ser Arg Thr Ser Arg Arg Lys Arg Tyr Ala Glu His Lys Ser
 130 135 140
 His Arg Gly Glu Tyr Ser Val Cys Asp Ser Glu Ser Leu Trp Val Thr
 145 150 155 160
 Asp Lys Ser Ser Ala Ile Asp Ile Arg Gly His Gln Val Thr Val Leu
 165 170 175
 Gly Glu Ile Lys Thr Gly Asn Ser Pro Val Lys Gln Tyr Phe Tyr Glu
 180 185 190

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Thr Arg Cys Lys Glu Ala Arg Pro Val Lys Asn Gly Cys Arg Gly Ile
 195 200 205
 Asp Asp Lys His Trp Asn Ser Gln Cys Lys Thr Ser Gln Thr Tyr Val
 210 215 220
 Arg Ala Leu Thr Ser Glu Asn Asn Lys Leu Val Gly Trp Arg Trp Ile
 225 230 235 240
 Arg Ile Asp Thr Ser Cys Val Cys Ala Leu Ser Arg Lys Ile Gly Arg
 245 250 255

Thr

<210> 7
 <211> 210
 <212> PRT
 <213> Homo sapiens

<400> 7
 Met Leu Pro Leu Pro Ser Cys Ser Leu Pro Ile Leu Leu Leu Phe Leu
 1 5 10 15
 Leu Pro Ser Val Pro Ile Glu Ser Gln Pro Pro Pro Ser Thr Leu Pro
 20 25 30
 Pro Phe Leu Ala Pro Glu Trp Asp Leu Leu Ser Pro Arg Val Val Leu
 35 40 45
 Ser Arg Gly Ala Pro Ala Gly Pro Pro Leu Leu Phe Leu Leu Glu Ala
 50 55 60
 Gly Ala Phe Arg Glu Ser Ala Gly Ala Pro Ala Asn Arg Ser Arg Arg
 65 70 75 80
 Gly Val Ser Glu Thr Ala Pro Ala Ser Arg Arg Gly Glu Leu Ala Val
 85 90 95
 Cys Asp Ala Val Ser Gly Trp Val Thr Asp Arg Arg Thr Ala Val Asp
 100 105 110
 Leu Arg Gly Arg Glu Val Glu Val Leu Gly Glu Val Pro Ala Ala Gly
 115 120 125
 Gly Ser Pro Leu Arg Gln Tyr Phe Phe Glu Thr Arg Cys Lys Ala Asp
 130 135 140
 Asn Ala Glu Glu Gly Gly Pro Gly Ala Gly Gly Gly Cys Arg Gly
 145 150 155 160
 Val Asp Arg Arg His Trp Val Ser Glu Cys Lys Ala Lys Gln Ser Tyr
 165 170 175
 Val Arg Ala Leu Thr Ala Asp Ala Gln Gly Arg Val Gly Trp Arg Trp
 180 185 190

09788188-07001

Ile Arg Ile Asp Thr Ala Cys Val Cys Thr Leu Leu Ser Arg Thr Gly
 195 200 205

Arg Ala
 210

<210> 8

<211> 210

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Mutant NT-4/5
 pro-neurotrophin

<400> 8

Met Leu Pro Leu Pro Ser Cys Ser Leu Pro Ile Leu Leu Leu Phe Leu
 1 5 10 15

Leu Pro Ser Val Pro Ile Glu Ser Gln Pro Pro Pro Ser Thr Leu Pro
 20 25 30

Pro Phe Leu Ala Pro Glu Trp Asp Leu Leu Ser Pro Arg Val Val Leu
 35 40 45

Ser Arg Gly Ala Pro Ala Gly Pro Pro Leu Leu Phe Leu Leu Glu Ala
 50 55 60

Gly Ala Phe Arg Glu Ser Ala Gly Ala Pro Ala Ser Arg Ser Arg Arg
 65 70 75 80

Gly Val Ser Glu Thr Ala Pro Ala Ser Arg Arg Gly Glu Leu Ala Val
 85 90 95

Cys Asp Ala Val Ser Gly Trp Val Thr Asp Arg Arg Thr Ala Val Asp
 100 105 110

Leu Arg Gly Arg Glu Val Glu Val Leu Gly Glu Val Pro Ala Ala Gly
 115 120 125

Gly Ser Pro Leu Arg Gln Tyr Phe Phe Glu Thr Arg Cys Lys Ala Asp
 130 135 140

Asn Ala Glu Glu Gly Gly Pro Gly Ala Gly Gly Gly Gly Cys Arg Gly
 145 150 155 160

Val Asp Arg Arg His Trp Val Ser Glu Cys Lys Ala Lys Gln Ser Tyr
 165 170 175

Val Arg Ala Leu Thr Ala Asp Ala Gln Gly Arg Val Gly Trp Arg Trp
 180 185 190

Ile Arg Ile Asp Thr Ala Cys Val Cys Thr Leu Leu Ser Arg Thr Gly
 195 200 205

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Arg Ala
210

<210> 9
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Recombinant
coding sequence for NGF

<400> 9
atgtccatgt tgttctacac tctgatcaca gcttttctga tcggcataca ggcggaacca 60
cactcagaga gcaatgtccc tgcaggacac accatcccc aagtccactg gactaaactt 120
cagcattccc ttgacactgc ctttcgcaga gcccgagcg ccccggcagc ggcgatagct 180
gcacgcgtgg cggggcagac ccgcaacatt actgtggacc ccaggctgtt taaaaagcgg 240
cgactccgtt caccctcgtg gctgttttag acccagcctc cccgtgaagc tgcagacact 300
caggatctgg acttcgaggt cgggtgtgct gccccttca acaggactca caggagcaag 360
cggtcacatc cccatcccat cttccacagg ggccaattct cgggtgtgtga cagtgtcagc 420
gtgtgggttg gggataagac caccgccaca gacatcaagg gcaaggaggt gatggtgttg 480
ggagagggtga acattaacaa cagtgtattc aaacagtact tttttgagac caagtgccgg 540
gacccaaatc ccgttgacag cgggtgccgg ggcattgact caaagcactg gaactcatat 600
tgtaccacga ctcacacctt tgtcaaggcg ctgaccatgg atggcaagca ggctgcctgg 660
cggtttatcc ggatagatac ggctgtgtg tgtgtgctca gcaggaaggc tgtgagaaga 720
gcctga 726

<210> 10
<211> 676
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Recombinant
coding sequence for NT-3 precursor

<220>
<221> modified_base
<222> (525)
<223> a, t, c, g, other or unknown

<220>
<221> modified_base
<222> (606)
<223> a, t, c, g, other or unknown

<220>
<221> modified_base
<222> (619)..(620)
<223> a, t, c, g, other or unknown

<220>
<221> modified_base
<222> (632)
<223> a, t, c, g, other or unknown

09788188-070901

<220>
 <221> modified_base
 <222> (643)
 <223> a, t, c, g, other or unknown

<400> 10
 ttggaaggca agcactga ttttattgag aaaaaagctt atatactgta ggggtgctga 60
 agtttaataa ataaagggtca acttataata tataaaaaaca atataaacat ttatatgcta 120
 catgcatatc atataattta aagtaataat ttatatatgg ggagagatgc caattcatgt 180
 tcttccgatt tttctcgaca aggcacacac acaggacgtg tctatccgta tccaccgcca 240
 gccacagagt ttattgttct ctgaagtcag tgctcggacg taggggtggg atgttttgca 300
 ctgagagttc cagtgtttat catcaatacc cctgcaaccg tttttgaccg gcctggcttc 360
 cttacatcgc gtttcataaa aatattgttt gacaggagag ttgccggtt tgatctcccc 420
 cagcaccgtg acctggtgtc cccgaatgtc gatggccgat gacttgcggt caccacaga 480
 ctctcactgt cacataccga gtactccct cggtgactct tatgnctcgc gtaccgtttt 540
 ccgccggatg ttctgttcgc caccacgggg cttgccacgt aatcctccat gagatacaag 600
 ggcggnggct cccaagggnn tgtgtcgctc ancaggaacc cgngtgagtg tagcggctct 660
 gttgtcgag aagttc 676

<210> 11
 <211> 468
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Recombinant
 coding sequence for NT-4 precursor

<400> 11
 ctggattcgg atcgacacag cttgcgtctg cagctcctc agccgaacag gccgagcctg 60
 aggtccaggc ttgggaactg cccaagttga gggaaaacaa aaaacaaaaa accaaagctg 120
 gatgctgaaa ggaccacagg ggtggcctgg ctgctctacc gtgccttatg actgggaact 180
 ggaataacca aagaatcaaa tctctctcaa atctcagtct gtgtggaatg tatgggtgaaa 240
 ccaaatgagg tttcaagtga tgaataggag ttctcccga ggaacttgac attaataaca 300
 atagccaatg tttactatct cctgtttatc agacctgata tatgactttg gcaaccattt 360
 taacattcag agaccctggc tcatcaaaac ggacgaggaa agaacgcatg aaaaggggat 420
 gcatgatgca tgcgctggag ctaggcctcc atcagtaggc tgtttctg 468

<210> 12
 <211> 633
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Recombinant
 coding sequence for NT-4/5

<400> 12
 atgctccctc tcccctcatg ctccctcccc atcctcctcc ttttctcct cccagtgctg 60
 ccaattgagt cccaaccccc accctcaaca ttgccccctt ttctggcccc tgagtgggac 120
 cttctctccc ccgagtagt cctgtctagg ggtgcccctg ctgggcccc tctgctcttc 180
 ctgctggagg ctggggcctt tcgggagtca gcagggtgcc cggccaaccg cagccggcgt 240
 ggggtgagcg aaactgcacc agcgagtcgt cggggtgagc tggctgtgtg cgatgcagtc 300
 agtggctggg tgacagaccg ccggaccgct gtggacttgc gtgggcgcga ggtggagggtg 360
 ttgggcgagg tgcctgcagc tggcgcgagt cccctccgcc agtacttctt tgaaaccgcg 420
 tgcaaggctg ataacgctga ggaaggtggc ccggggggcag gtggaggggg ctgccgggga 480

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<220>
<223> Description of Artificial Sequence: Recombinant
DNA

<400> 16

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atgtccatgt tgttctacac tctgatcaca gcttttctga tcggcataca ggcggaacca 60
cactcagaga gcaatgtccc tgcaggacac accatcccc aagtccactg gactaaactt 120
cagcattccc ttgacactgc ctttcgcaga gcccgagcg ccccggcagc ggcgatagct 180
gcacgcgtgg cggggcagac ccgcaacatt actgtggacc ccaggctgtt taaaaagcgg 240
cgactccgtt caccctgtgt gctgttttagc acccagcctc cccgtgaagc tgcagacact 300
caggatctgg acttcgaggt cgggtggtgct gcccccttca gcaggactca caggagcaag 360
cggtcacat cccatcccat cttccacagg ggcgaattct cgggtgtgtga cagtgtcagc 420
gtgtgggttg gggataagac caccgccaca gacatcaagg gcaaggaggt gatggtgttg 480
ggagaggtga acattaacaa cagtgtattc aaacagtact tttttgagac caagtgccgg 540
gacccaaatc ccgttgacag cgggtgccgg ggcattgact caaagcactg gaactcatat 600
tgtaccacga ctcacacctt tgtcaaggcg ctgaccatgg atggcaagca ggctgcctgg 660
cggtttatcc ggatagatac ggccctgtgtg tgtgtgctca gcaggaaggc tgtgagaaga 720
gcctga 726

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